

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Marvin J. Slepian

Serial No.: 10/072,766

Art Unit: 1633

Filed: February 8, 2002

Examiner: Maria Marvich

For: *ENDOMURAL THERAPY*

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUBSTITUTE APPEAL BRIEF

Sir:

This is an appeal from the Office Action mailed on August 10, 2007, revised in view of the Notice of Non-Compliant Appeal Brief mailed May 15, 2008. Enclosed with this Appeal Brief is a Petition for an Extension of Time for Four Months, up to and including October 15, 2008. The Commissioner is hereby authorized to charge the fee for a small entity, to Deposit Account No. 50-3129. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

(1) REAL PARTY IN INTEREST

The real party in interest of this application is the inventor, Dr. Marvin Slepian, and the assignee, Endoluminal Therapeutics.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

(3) STATUS OF CLAIMS

Claims 1, 3, 6-13, 15-33, and 35-37 are pending. Claims 2, 4, 5, 14, and 34 have been cancelled. Claims 8-12, 26, 27, and 30 are withdrawn. Claims 1, 3, 6, 7, 13, 15-25, 28-33, and 35-37 are on appeal. The text of each claim on appeal, as pending, is set forth in an Appendix to this Appeal Brief.

(4) STATUS OF AMENDMENTS

The claims were last amended in an Amendment filed via facsimile transmission on November 14, 2007, as indicated in the Advisory Action mailed on December 12, 2007. An appendix sets forth the claims on appeal.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

Independent claims 1, 15, and 25 are discussed below.

Claim 1 is drawn to a method of treatment comprising

- (a) penetrating into the endomural zone of an organ, organ component or tissue structure,
- (b) cutting or removing tissue in the endomural zone to create a void, cavity, containment

space or reservoir area, and

(c) delivering a therapeutic, prophylactic or diagnostic agent to the void, cavity, containment space or reservoir area in the endomural zone, wherein the agent is in a polymeric material for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent to the endomural zone,

wherein the polymeric material is selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, and combinations thereof. Support for each of the claimed elements are found at least at page 7, 8, 9 at lines 13-26, page 12 at line 12 to page 13 at line 6, page 14; pages 23-25.

Claim 3 defines the therapeutic, prophylactic or diagnostic agent as drugs or cells. Claim 6 defines the drugs as anti-infectives, antibiotics, antifungal, antihelminthic, antiparasitic agents, anticancer agents, anti-proliferative agents, anti-migratory agents, anti-inflammatory agents, metalloproteases, proteases, thrombolytic agents, fibrinolytic agents, steroids, hormones, vitamins, carbohydrates, lipids proteins, peptides and enzymes. Claim 7 defines the drugs as proliferative growth factors selected from the group consisting of platelet derived growth factor (PDGF), fibroblast growth factor (FGF), transforming growth factor (TGF), eye-derived growth factor (EDGF), epidermal growth factor (EGF), nerve growth factor (NGF), insulin-like growth factor (ILGF), vascular endothelial growth factor (VEGF), Hepatocyte scatter factor, angiogenic growth factors, serum factors, collagen, laminin, tenascin, secreted protein acidic and rich in cysteine (SPARC), thrombospondin, fibronectin, vimentin and other matrix factors. Claim 13 defines the therapeutic agent as heat shock proteins, stress response proteins, and inducers of

heat shock or stress response proteins. Claim 35 defines the method, wherein the organ, organ component or tissue structure is penetrated percutaneously, surgically, or via endoluminal entry. Claim 36 defines the method of claim 1 wherein the means for delivery of a therapeutic, prophylactic or diagnostic agent is a tubular device. Claim 37 defines the method wherein the tubular device is a catheter, syringe or spray device.

Claim 15 defines a device comprising

a hollow tubular member with an end means for creating a void, cavity, containment space or reservoir area in the endomural zone of an organ, organ component or tissue structure, by cutting or removal of tissue, wherein the means for creating the void, cavity, containment space or reservoir area is designed to cause minimal collateral damage to tissue surrounding a site where the void, cavity, containment space or reservoir is created,

and means for local delivery of a therapeutic, prophylactic or diagnostic agent into the void, cavity, containment space or reservoir area, wherein the agent is delivered in a polymeric carrier selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, and combinations thereof,

the device further comprising means for indirect or direct guidance.

Support for claim 15 is found at least at page 9, line 20 to page 10, line 29; Figures 3-5.

Claim 16 defines the device wherein the member is rigid and made of metal, polymer, or composite. Claim 17 defines the device wherein the member is a flexible tubular tissue accessing device. Claim 18 defines the device wherein the device further comprises means for

containment and local delivery of the therapeutic, prophylactic or diagnostic agent attached to the member. Claim 19 defines the device wherein the means to create the void, cavity, containment space or reservoir comprises an expansile cutter attached to an end of the member. Claim 20 defines the device as further comprising diagnostic or therapeutic sensors. Claim 21 defines the device as further comprising projectile means to ballistically transfer particles through the ectoluminal or endoluminal zone for retention in the endomural zone. Claim 22 defines the projectile means as mechanical acceleration, electrical transfer, spark explosion, and gas explosion. Claim 23 defines the device as further comprising means for direct guidance. Claim 24 defines the device wherein the means for direct guidance is selected from the group consisting of fiber optic imaging systems, endoscopes, direct tip cameras, charge coupled device (CCD), Complimentary Metal Oxide Semiconductor (C-MOS) or other chip or electrical video systems, and ultrasound or global positioning systems (GPS). Claim 31 defines the device wherein the device is suitable for nerve regeneration.

Claim 25 defines a kit comprising

a device comprising

a hollow tubular member with an end means for penetrating into the endomural zone of an organ, organ component or tissue structure,

a means for creating a void, cavity, containment space or reservoir area in the endomural zone, wherein the means for creating a void is designed to cause minimal collateral damage to

tissue surrounding a site where a void is created, further comprising means for indirect or direct guidance, and

means for local delivery of therapeutic, prophylactic or diagnostic agents into the void, cavity, containment space or reservoir area, and

a void filling polymeric material or implant, wherein the void filling material or implant is in a form suitable for local delivery. See original claims; same disclosure as for claim 1 (Support for each of the claimed elements are found at least at page 7, 8, 9 at lines 13-26, page 12 at line 12 to page 13 at line 6, page 14; pages 23-25) and claim 15 (Support for claim 15 is found at least at page 9, line 20 to page 10, line 29; Figures 3-5).

Claim 28 defines the kit as further comprising a therapeutic for induction of angiogenesis or myogenesis. Claim 29 defines the kit wherein the therapeutic is angiogenic growth factors, inflammatory angiogenic polymers or polymer constructs, or electroactive or other microinjurious or locally stimulatory polymers. Claim 32 further defines the kit as comprising a bioactive polymer. Claim 33 defines the kit as further comprising stress response inducing agents or stress response proteins.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

(a) Whether claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are disclosed under 35 U.S.C. 102(e) by U.S. Patent No. 6,585,716 to Altman.

(b) Whether claims 1, 3, 6, 7, 15-19, 21-23, 25, 34, 36 and 37 are disclosed under 35 U.S.C. 102(e) by U.S. patent No. 6,102,887 to Altman.

(c) Whether claims 1, 3, 6, 7, 14-16, 18, 20-24, 32, and 34-37 are disclosed under 35 U.S.C. 102(e) by U.S. Patent No. 6,309,370 to Haim, et al.

(d) Whether claims 13 and 33 are obvious under 35 U.S.C. in view of U.S. Patent No. 6,585,716 to Altman or U.S. Patent No. 6,102,887 to Altman or U.S. Patent No. 6,309,370 to Haim, et al. in view of Benjamin and McMillan, Circ. Res. 83, 117-132 (1998).

(e) Whether claim 31 is obvious under 35 U.S.C. 103 over Brosamle, et al., J. Neurosci. 20:21, 8061-8068 (2000) in view of U.S. Patent No. 6,585,716 to Altman or U.S. Patent No. 6,102,887 to Altman or U.S. Patent No. 6,309,370 to Haim, et al.

(7) Argument

(a) The Claimed Invention

The claims are drawn to a method, and a device and kit for use with the method. The method requires the following steps:

- (1) penetrating into by cutting or removal of tissue the endomural zone of a tissue,
- (2) with a means for delivery of a therapeutic, prophylactic or diagnostic agent,
- (3) delivering the therapeutic, prophylactic or diagnostic agent into the stie of cutting or tissue removal,
- (4) where the agent is in a form for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent,
- (5) where the agent is delivered in a polymeric material.

The examiner is correct that the heart includes an endomural zone, between the outer layer and the inner lumen. This is how the endomural zone is defined in appellant's specification.

Spinal cord is not a tissue, but many nerves that are "packaged" together. This does not fit into the definition at page 5 of tissue components which are organized into organs, requiring multiple integrated and interactive tissue components. The endomural zone is defined at page 6 as a region in an organ.

Accordingly, the examiner is correct that there is an endomural zone within the tissue forming the heart; the examiner is not correct to the extent it is alleged that the spinal cord has an endoluminal zone.

(b) Rejections Under 35 U.S.C. § 102

Claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,585,716 by Altman ("the '716 patent"). Claims 1, 3, 6, 7, 15-19, 21-23, 25, 34, 36 and 37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,102,887 by Altman ("the '887 patent"). Claims 1, 3, 6, 7, 14-16, 18, 20-24, 32 and 34-37 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent").

(I) Claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are not anticipated by U.S. Patent No. 6,585,716 by Altman ("the '716 patent").

The '716 patent describes methods for treating the human heart. A guide catheter is placed in the venous portion of a patient's vasculature and extends until the vena cava and coronary sinus. A drug delivery catheter is inserted inside the guide catheter and extends beyond the guide catheter so that the tip enters the cardiac vein and extends to the posterior vein. The tip contains a penetrating element, such as a curved or helical needle, that is selectively extended into the wall of the vein and into the myocardium. Therapeutic agents are injected into the myocardium, through the needle (col. 4, lines 5-19 and Figure 1). The guide catheter contains an occluding mechanism. The venous flow path is shut off by occluding the coronary ostium with the occluding mechanism. This stops the natural blood flow from the myocardium into the vein, thereby preventing the therapeutic agents from being flushed out of the myocardium in the course of normal blood flow. (col. 4, lines 20-47)

The '716 patent does not disclose forming a void, cavity, containment space or reservoir area in the endomural zone as required by amended claims 1, 15 and 25. The '716 patent merely uses a catheter which is inserted between cells into the heart tissue for delivery of drug to the vasculature within the heart. This is a pre-existing structure. There is no teaching to create a new void, cavity, containment space or reservoir area by cutting or other means permanently removing the tissue. Insertion of a needle or catheter does not create a void as claimed, but

merely pushes aside tissue which refills the temporary displacement upon removal of the device. Catheters and needles do not cut or remove tissue; they simply displace it.

The examiner states that because appellant has stated that needles or catheters can be used, the device in Altman must perform the same function. This is not the case. A needle or catheter, of an appropriate bore size, can be used to remove tissue; a needle of a smaller size, only displaces tissue, not remove tissue.

Altman does not create a void into which a polymeric material is implanted. Altman injects into the tissue a dispersion of particles for drug delivery. Altman disperses particles throughout the tissue. This is very clear by reference to col. 4. A catheter is used to pass through blood vessels into the inferior vena cava, from which a needle (note the significantly smaller size) is used to inject (and the use of the word “inject”, line 18) particles into the myocardium. Steps have to then be taken so that the particles are retained (line 20 of col. 4, see also col. 5, lines 16-38) - if there was void or containment region created, no additional steps to retain the particles at the site would be required. This statement alone differentiates the method of the ‘716 patent from the claimed method. See also col. 5, lines 56-60.

In summary, Altman’s method is not the same as that of appellant based on at least two differences:

Altman does not use a means for cutting or creating a void;

Altman does not put into the void a polymeric material which is retained within the void.

Altman instead injects into the tissue, not removing any tissue, which causes problems with retention, since the tissue has merely been pushed aside by the needle, and therefore squeezes back to its previous shape when the needle is withdrawn, trying to expel the drug.

Altman also does not disclose projectile means, expansile cutter means, or a void filling material.

Therefore, claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are novel over the '716 patent.

Claim 20 is novel over the '716 patent

The '716 patent does not disclose a device including a diagnostic or therapeutic sensor. Therefore claim 20 is novel over the '716 patent.

Claims 21-22, are novel over the '716 patent

The '716 patent fails to disclose projectile means to transfer particles through the ectoluminal or endoluminal zone. At most, the '716 patent discloses a catheter through which a solution or suspension is passaged by mechanical pressure.

Claim 23 is novel over the '716 patent

The '716 patent fails to disclose a device for direct guidance of the device as claimed in claim 15, as the examiner has recognized in not rejecting claim 24, which defines what a means for direct guidance is.

(2) Claims 1, 3, 6, 7, 15-19, 21-23, 25, 34, 36 and 37 are not anticipated by

U.S. Patent No. 6,102,887 by Altman ("the '887 patent").

The '887 patent describes a steerable catheter with a deployable penetrating element, such as a helical or straight needle, for administration of drugs to the heart (col. 3, lines 9-22). Agents can be delivered in microformulations such as microspheres, nanoparticles or polymers. The claims, as amended require creating a void, cavity, containment space or reservoir area in the endoluminal zone by cutting or removal of tissue. The '887 patent merely uses a catheter with a distensible needle for delivery of drugs to the myocardium of the heart. There is no teaching to create a new void, cavity, containment space or reservoir area by cutting or any other means which permanently remove the tissue. As discussed above with respect to the '716 patent, insertion of a needle or catheter does not create a void as claimed, but merely pushes aside tissue which refills the temporary displacement upon removal of the device. Catheters and needles do not cut or remove tissue; they simply displace it.

Col. 9, lines 20-52 discloses an expanding prong *fixation* system, which may be used to *stabilize* the needle, *not* to create a void, cavity, containment space or reservoir as required by independent claims 1, 15 and 25. Merriam-Webster defines "void" as "not occupied" or "containing nothing". Merriam-Webster also defines "cavity" as "an unfilled space within a mass" (*see* definition attached). The instant claims require the formation of such an "*unfilled* space", into which the therapeutic, prophylactic or diagnostic agent is delivered. Although the prong fixation system disclosed in the '887 patent is able to penetrate body tissue, this merely

creates a cut in the tissue which is *occupied*, or *filled* with the prongs. The fixation system is designed to stay in place as the agent is delivered. The '887 patent does not disclose retracting the prongs prior to delivery of an agent. Thus, the prongs of the fixation system disclosed in the '887 patent do not create a void, cavity, containment space or reservoir into which the agent is delivered.

In col. 2, Altman makes clear that the prior art describes a variety of means for infusing the heart. All of these are referred to as penetrating needles or catheters, and that his improvement is the addition of steering and fixation means. The summary reinforces the argument that the delivery is by injection into the tissue NOT creation of a void into which polymeric material is implanted. IF the needle were removing tissue, then there would have to be some means to dispose of the tissue prior to using the same needle to inject drug. There is none. IF the needle were used to create a void, the lumen of the needle would be filled with tissue; no drug could pass through into the space. However, this clearly does not happen because no tissue is removed, no void is created. Therefore, Altman '887 does not anticipate the claimed methods and claims 1, 3, 6, 7, 15-18, 19, 21-23, 25, 34, 36 and 37 are novel over the '887 patent.

Claims 21-22, are novel over the '887 patent

The '887 patent fails to disclose projectile means to transfer particles through the ectoluminal or endoluminal zone. At most, the '887 patent discloses a catheter through which a solution or suspension is passaged by mechanical pressure.

Claim 23 is novel over the '887 patent

The '887 patent fails to disclose a device for direct guidance of the device as claimed in claim 15, as the examiner has recognized in not rejecting claim 24, which defines what a means for direct guidance is.

(3) Claims 1, 3, 6, 7, 14-16, 18, 20-24, 32 and 34-37 are not anticipated by

U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent").

The '370 patent discloses a method and device for delivery of growth factors to an ischemic region in the heart. The '370 patent emphasizes the importance of navigating the catheter to the site of the ischemic regions (see col. 4, lines 25-40). The device is a catheter that contains sensors to determine the position of the catheter with respect to the heart wall (col. 12, lines 10-28). When the device is in place, the needle is placed inside the heart wall and the growth factors are delivered (see e.g. col. 12, lines 40-49 and col. 13, lines 39-50 and col. 14, lines 3-11). The growth factors may be administered in a solution or a capsule (see col. 15, lines 14-20).

As discussed above with respect to the '716 and '887 patents, the '370 patent does not disclose forming a void, cavity, containment space or reservoir area in the **endomural** zone, as required by amended claims 1, 15 and 25. The '370 patent merely uses a catheter for delivery of drug to the vasculature within the heart.

Claim 20 is novel over the '370 patent

The '370 patent does not disclose a device including a diagnostic or therapeutic sensor. Therefore claim 20 is novel over the '370 patent.

Claims 21-22, are novel over the '370 patent

The '370 patent fails to disclose projectile means to transfer particles through the ectoluminal or endoluminal zone. At most, the '370 patent discloses a catheter through which a solution or suspension is passaged by mechanical pressure.

Claim 23 is novel over the '3706 patent

The '370 patent fails to disclose a device for direct guidance of the device as claimed in claim 15, as the examiner has recognized in not rejecting claim 24, which defines what a means for direct guidance is.

(4) Summary

As discussed above, none of these reference disclose creating a void and then filling it.

Moreover, none of the references disclose creating a void in the endomural zone. The examiner has stated that the region that is treated must be the endomural zone, but has provided no evidence that this would inherently be the case. Inherence requires more than the mere possibility; it must be the case. All of these methods are designed to deliver drug to a particular area of the heart, usually one that has been damaged due to ischemia. There is no indication that this region would be, or even principally be, the endomural zone.

In summary, the prior art does not anticipate the claims because it does not teach creation of a void; filling of a void with a polymeric material.

Moreover, none of these references would also anticipate because the claims no longer encompass delivery of micro or nanoparticles.

(c) Rejection Under 35 U.S.C. § 103

Claims 13 and 33 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 6,585,716 by Altman (“the ‘716 patent”) or U.S. Patent No. 6,102,887 by Altman (“the 887 patent”) or U.S. Patent No. 6,309,370 by Haim, *et al.* (“the ‘370 patent”), in view of Benjamin and McMillan, *Circ. Res.*, 83:117-132 (1988) (“Benjamin and McMillan”). Claim 31 was rejected under 35 U.S.C. § 103(a) as obvious over Brosamle, *et al.*, *The Journal of Neuroscience*, 20(21):8061-68 (“Brosamle”) in view of U.S. Patent No. 6,585,716 by Altman (“the ‘716 patent”) or U.S. Patent No. 6,102,887 by Altman (“the 887 patent”) or U.S. Patent No. 6,309,370 by Haim, *et al.* (“the ‘370 patent”).

The claims, Altman ‘716, Altman ‘887 and Haim have been discussed above. The claimed method requires creation of a void and filling of the void with a polymeric material. Altman and Haim describe displacement and the use of remedial measures involving physical displacement to keep the injected drugs within the site of injection. This teaches away from what appellant claims.

(I) Claims 13 and 33 are not obvious over the combination of the ‘716, ‘887, or ‘370 patents with Benjamin

Claims 13 and 33 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 6,585,716 by Altman (“the ‘716 patent”) or U.S. Patent No. 6,102,887 by Altman (“the 887 patent”) or U.S. Patent No. 6,309,370 by Haim, *et al.* (“the ‘370 patent”), in view of Benjamin and McMillan, *Circ. Res.*, 83:117-132 (1988) (“Benjamin and McMillan”). As noted above, none of the ‘716, ‘887 or ‘370 patents disclose a means for forming a void, cavity, containment space or reservoir area in the endomural zone by cutting or removing tissue. Additionally, the ‘370 patent does not disclose including a void filling material or implant in the device.

Benjamin is a general reference about heat shock proteins and some of their roles. Benjamin does not cure the deficiencies of the ‘716, ‘887, and ‘370 patents. The combination of these references still does not disclose or suggest delivering heat shock proteins, stress response proteins, and inducers of heat shock or stress response proteins into a void, cavity, containment space or reservoir area created by cutting or removal of tissue as defined by claim 13. Additionally, the combination of Benjamin with the ‘716, ‘887, and ‘370 patents does not disclose a kit containing a void filling material or implant in a form suitable for local administration, as required by claim 33.

(2) Claim 31 is not obvious over Brosamle, *et al.*, The Journal of Neuroscience, 20(21):8061-68 ("Brosamle") in view of U.S. Patent No. 6,585,716 by Altman ("the '716 patent") or U.S. Patent No. 6,102,887 by Altman ("the 887 patent") or U.S. Patent No. 6,309,370 by Haim, *et al.* ("the '370 patent").

Claim 31 is device claim that depends from claim 15 and further defines the device as being suitable for nerve regeneration.

The combination of Brösamle with Altman '716, Altman '887, or Haim

As noted above, the '716, '887 and '370 patents do not disclose forming a void, cavity, containment space or reservoir area in the endomural zone by cutting or removing tissue, as required by claim 31. Brösamle describes administering an antibody to the spinal cord to promote regeneration. Brösamle does not cure the deficiencies of the '716, '887 or '370 patents. Brösamle does not disclose a device with means for for creating a void, cavity, containment space or reservoir area. Therefore the combination of Brösamle with the '716, '887, or '370 patents does not make claim 31 obvious.

Allowance of claims 1, 3, 6, 7, 13, 15-25, 28, 29, 31-33 and 35-37 is respectfully solicited.

Respectfully submitted,

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APPENDIX: CLAIMS

1. A method of treatment comprising
 - (a) penetrating into the endomural zone of an organ, organ component or tissue structure,
 - (b) cutting or removing tissue in the endomural zone to create a void, cavity, containment space or reservoir area, and
 - (c) delivering a therapeutic, prophylactic or diagnostic agent to the void, cavity, containment space or reservoir area in the endomural zone, wherein the agent is in a polymeric material for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent to the endomural zone,wherein the polymeric material is selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, and combinations thereof.

Claim 2. (canceled)

3. The method of claim 1 wherein the therapeutic, prophylactic or diagnostic agent is selected from the group consisting of drugs and cells.

Claim 4. (canceled)

Claim 5. (canceled).

6. The method of claim 3 wherein the drugs are selected from the group consisting of anti-infectives, antibiotics, antifungal, anthelmintic, antiparasitic agents, anticancer agents, anti-proliferative agents, anti-migratory agents, anti-inflammatory agents, metalloproteases,

proteases, thrombolytic agents, fibrinolytic agents, steroids, hormones, vitamins, carbohydrates, lipids proteins, peptides and enzymes.

7. The method of claim 3 wherein the drugs are proliferative growth factors selected from the group consisting of platelet derived growth factor (PDGF), fibroblast growth factor (FGF), transforming growth factor (TGF), eye-derived growth factor (EDGF), epidermal growth factor (EGF), nerve growth factor (NGF), insulin-like growth factor (ILGF), vascular endothelial growth factor (VEGF), Hepatocyte scatter factor, angiogenic growth factors, serum factors, collagen, laminin, tenascin, secreted protein acidic and rich in cysteine (SPARC), thrombospondin, fibronectin, vimentin and other matrix factors.

8. (withdrawn) The method of claim 3 wherein the cells are autogenous similar cells from adjacent normal zones of the same or different organs.

9. (withdrawn) The method of claim 3 wherein the cells are autogenous differing cells from adjacent normal zones of the same or different organs.

10. (previously presented; withdrawn) The method of claim 3 wherein the cells are stem cells or other progenitor cells.

11. (withdrawn) The method of claim 3 wherein the cells are explanted and expanded *in vitro* for implantation.

12. (previously presented; withdrawn) The method of claim 1 wherein the therapeutic agent is selected from the group consisting of genes, plasmids, episomes, viruses, and viroids.

13. The method of claim 3 wherein the therapeutic agent is selected from the group consisting of heat shock proteins, stress response proteins, and inducers of heat shock or stress response proteins.

Claim 14. (canceled)

15. A device comprising
a hollow tubular member with an end means for creating a void, cavity, containment space or reservoir area in the endomural zone of an organ, organ component or tissue structure, by cutting or removal of tissue, wherein the means for creating the void, cavity, containment space or reservoir area is designed to cause minimal collateral damage to tissue surrounding a site where the void, cavity, containment space or reservoir is created,

and means for local delivery of a therapeutic, prophylactic or diagnostic agent into the void, cavity, containment space or reservoir area, wherein the agent is delivered in a polymeric carrier selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, and combinations thereof,

the device further comprising means for indirect or direct guidance.

16. The device of claim 15 wherein the member is rigid and made of metal, polymer, or composite.

17. The device of claim 15 wherein the member is a flexible tubular tissue accessing device.

18. The device of claim 15 wherein the device further comprises means for containment and local delivery of the therapeutic, prophylactic or diagnostic agent attached to the member.
19. The device of claim 15 wherein the means to create the void, cavity, containment space or reservoir comprises an expansile cutter attached to an end of the member.
20. The device of claim 15 further comprising diagnostic or therapeutic sensors.
21. The device of claim 15 further comprising projectile means to ballistically transfer particles through the ectoluminal or endoluminal zone for retention in the endomural zone.
22. The device of claim 21 wherein the projectile means is selected from the group comprising mechanical acceleration, electrical transfer, spark explosion, and gas explosion.
23. The device of claim 15 further comprising means for direct guidance.
24. The device of claim 23 wherein the means for direct guidance is selected from the group consisting of fiber optic imaging systems, endoscopes, direct tip cameras, charge coupled device (CCD), Complimentary Metal Oxide Semiconductor (C-MOS) or other chip or electrical video systems, and ultrasound or global positioning systems (GPS).
25. A kit comprising
a device comprising
a hollow tubular member with an end means for penetrating into the endomural zone of an organ, organ component or tissue structure,

a means for creating a void, cavity, containment space or reservoir area in the endomural zone, wherein the means for creating a void is designed to cause minimal collateral damage to tissue surrounding a site where a void is created, further comprising means for indirect or direct guidance, and

means for local delivery of therapeutic, prophylactic or diagnostic agents into the void, cavity, containment space or reservoir area, and

a void filling polymeric material or implant, wherein the void filling material or implant is in a form suitable for local delivery.

26. (withdrawn) The kit of claim 25 wherein the void filling material or implant can locally sense, store or telemeter physical, chemical or biological information.

27. (withdrawn) The kit of claim 25 comprising electroactive or electroconductive polymers which may be directly or externally activated via transcutaneous energy delivery to elicit positive or negative galvanotaxis.

28. The kit of claim 25 further comprising a therapeutic for induction of angiogenesis or myogenesis.

29. The kit of claim 28 wherein the therapeutic is selected from the group of angiogenic growth factors, inflammatory angiogenic polymers or polymer constructs, and electroactive or other microinjurious or locally stimulatory polymers.

30. (withdrawn) The kit of claim 28 wherein the therapeutic comprises cells selected from the group consisting of endothelial cells, EC bone marrow precursor cells, other stems cells

smooth muscle cells or precursors, combinations, neural cells or neural stem cells or combinations thereof.

31. The device of claim 15, wherein the device is suitable for nerve regeneration.

32. The kit of claim 25 comprising a bioactive polymer.

33. The kit of claim 25 further comprising stress response inducing agents or stress response proteins.

Claim 34. (canceled)

35. The method of claim 1, wherein the organ, organ component or tissue structure is penetrated percutaneously, surgically, or via endoluminal entry.

36. The method of claim 1 wherein the means for delivery of a therapeutic, prophylactic or diagnostic agent is a tubular device.

37. The method of claim 1, wherein the tubular device is selected from the group consisting of catheters, syringes and spray devices.

APPENDIX:

There are no related proceedings or appeals that the undersigned is aware of that would have any bearing on the outcome in this appeal.

APPENDIX:

No evidence beyond the application as filed and the references cited during prosecution are in evidence in this application.